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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/542,885

01/06/2006

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0643418

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08/19/2010

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EXAMINER

KASSA, TIGABU

ART UNIT

PAPER NUMBER

1619

NOTIFICATION DATE

DELIVERY MODE

08/19/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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nyuspatactions@ladas.com

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DETAILED ACTION

Formal Matters

Applicants' amendment filed on 06/28/2010 is acknowledged and entered. **Claims 2-18 are pending. Claims 2-12 and 18 are under consideration in the instant office action.** Claims 13-17 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claims. Claim 1 is cancelled. Applicants' amendment to the specification necessitated a new ground of objection. This Office Action is FINAL.

Corrected Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Applicants' claim of foreign priority to CHINA 03130709 is DENIED because no translation of the Chinese language document has been provided. Benefit is accorded to PCT/CN04/00409, filed on 04/27/2004.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 01/15/10 is noted and the submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the references. A signed copy is attached.

New Objections

Specification Objection

The appendix to the specification filed on 06/28/10 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original

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disclosure is as follows: Applicants' have filed a comparison data on 06/28/10 as an appendix to the specification. Applicants are required to cancel the link of the comparison data to the specification since it presents a new matter to the original disclosure in the reply to this Office Action. Applicants' may file the comparison data in the form of affidavit or declaration.

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

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Claims 2-12 and 18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Gai et al. (CN1273114, IDS reference) in view of Su et al. (US Patent 4,968,675), for the reasons of record and the reasons set forth herein.

Response to arguments

Applicants' arguments filed on 06/28/2010 have been fully considered but they are not persuasive.

Applicants argue that the key sentence in the official action seems to be "Although the compound taught by Suet al. is not the same as the instantly claimed compound (i.e. the compound taught by Gai et al), it is sufficiently similar as to provide valuable and relevant guidance to the skilled artisan in determining the types and amounts of buffers to use."

The examiner made a similar argument in response to the previous action. The applicant disagreed pointing out Su is concerned with salts of 16.alpha.-methyl-21-[4-[2,6-bis(1-pyrrolidinyl)-4-pyrimidinyl]-1-piperazin yl]pregna-1,4,9(11)-triene-3,20-dione In order to achieve this, Su turned to teachings relating to Ellipticine (5,11-Dimethyl-6/-pyrido[4,3-b]carbazole). These are both nitrogen-containing compounds. There is, however, no reason to think that teaching relating to either of these compounds is relevant to saponins obtained from notogiseng. Saponin RG 1 referred to in the examples of the present application does not contain nitrogen. It was therefore argued that there was no real basis for combining the teachings of Gai and Su. The examiner makes no substantive comment on these points but rather just argues that "even without the teachings of Su" the invention would be obvious. If this is the examiner's position, he should cite some alternative reference to Su to substantiate his position.

Applications should not be rejected simply on the basis of unsupported assertions of the examiner. The examiner needs to explain the basis of the rejection and the factual basis for it. In re Ahlert, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970).

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This is not found persuasive because applicants' resorted to attacking the references individually while the rejection is based on the combined teachings of Gai et al. and Su et al. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). For Su et al. to be a proper prior art to be combined with Gai et al. Su et al. do not necessarily have to teach exactly the same compounds as Gai et al. As it is clearly explained in the previous office action Su et al. is incorporated in the rejection for curing the deficiencies of Gai et al. **for not teaching the inclusion of an iso-osmotic solution, how the pH of the injection is regulated, and for not specifying concentration of the components** not for the saponin powder of notoginseng. The limitation of the saponin powder of notoginseng is clearly met and addressed by the teachings of Gai et al. as set forth in the previous office action. Because Su et al. teach the use of an iso-osmotic solution and pH regulator and their concentrations in formulating similar pharmaceutical formulation, it would have been obvious to one of ordinary skill in the art to apply the teachings of Su et al. to the similar composition of Gai et al. In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found **either in the references themselves or in the knowledge generally available to one of ordinary skill in the art**. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). Furthermore, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. **It is not necessary that the prior art suggest the combination to achieve the same advantage or**

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result discovered by applicant. See, e.g., *In re Kahn*, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed.Cir. 2006).

Applicants also assert that the examiner's insistence that the compounds of Gai and Su are sufficiently similar that teaching relating to compositions containing one would be relevant to compositions containing the other, both of them are steroid derivatives, but this is the end of the similarity. They do not have the same structures; thus, persons skilled in the art would not have been motivated to apply the buffer and isotonic solution as taught in Su et al into the product of Gai et al. (i.e., Xuesaitong injection). Steroid derivatives are general name of a variety of derivatives which are broadly distributed in nature and cover numerous substances, and it is well known that substances covered by the term "steroid derivatives" may be substantially different one another in terms of structure and physico-chemical property. For instance, ellipticine differs remarkably from the major active ingredients of saponins obtained from Panax notoginseng (e.g., Rgl, Rbl, RJ and the like) in structures, physico-chemical properties, and physiological activities, and thus they are not compounds having similar properties. In this situation, persons skilled in the art cannot conclude reasonably that a buffer suitable for ellipticine is also suitable for saponins obtained from Panax notoginseng. Thus, referring to Su et al as proposed by the examiner is not reasonable and persons skilled in the art have not been motivated to combine Gai et al with Su et al.

This is not found persuasive because for Gai et al. and Su et al. to be combinable they do not have to teach exactly the same structures. The fact that they teach compositions containing steroid derivatives by it self as admitted by applicants is sufficient enough to combine the references. See, for example, *Ex parte Bland*, 3 USPQ2d 1103 (Bd. Pat App. & Inter. 1986) (Claims were drawn to a particulate composition useful as a preservative for an animal foodstuff (or a method of inhibiting fungus growth in an animal foodstuff therewith) comprising verxite having absorbed thereon propionic acid. All references were concerned with absorbing biologically active materials on carriers, and therefore the teachings in

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each of the various references would have been pertinent to the problems in the other references and the invention at hand.). Therefore, even without the teachings of Su et al., the use of a physiological buffer and isotonic solutions for regulation of pH and making the solution physiologically compatible would have been obvious to the skilled artisan since the composition of Gai et al. is designed for injection. The rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. KSR, 550 U.S. at ___, 82 USPQ2d at 1395; Sakraida v. AG Pro, Inc., 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); Anderson 's-Black Rock, Inc. v. Pavement Salvage Co., 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). “[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” KSR, 550 U.S. at ___, 82 USPQ2d at 1396. In the instant case the use of physiological buffers and isotonic solutions for the preparation of injectable formulations are commonly known in the art as also demonstrated by Su et al.

Applicants also argue that as for the boiling and pasteurization at 110°C step of the present application, the applicant submits respectfully that the boiling step of the claimed method is conducted prior to the addition of Panax notoginseng saponin family powders, and thus it would not affect the stability of Panax notoginseng saponins. Moreover, the step of pasteurization at 110°C is conducted after the injection is put in the fluid infusion bottle and capped. That is to say, the pasteurization step is conducted in a sealed contained, and thus would not cause any undesired reaction affecting the content of saponins, such as, oxidation. However, the boiling step of Gai et al is conducted in an open container for a period of up to 15-20 minutes. During this period, it is certain that the solvent is substantially evaporated and some undesired reactions (e.g., oxidation of saponins) are likely to occur in the system

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because of high temperature and exposure to air such that the content of active ingredients of the injection is reduced. It can be seen that the present application avoids the potential loss of active ingredients and uncertain change of pH.

This is not found persuasive because applicants' assertion is based on speculation not objective evidence. Applicants' assertion is may be true but the burden of establishing, the burden of establishing non-obviousness by objective evidence is on Applicants showing that the boiling step implemented by Gai et al. would result in the undesired reactions applicants' allege. Gai. Et al. however clearly teach that the final product they produced after implementing all the steps including boiling resulted in a product with high transparency and long storage period which is an indication that their product did not undergoes the oxidation that applicants' allege. Additionally, applicants are using a product-by process format regarding to instant claim 18. The 35 USC 103 rejection set forth in the previous office action is proper because the product-by-process format that applicant incorporated does not impart any structural difference with the prior art product. Please note that in product-by-process claims, "once a product appearing to be substantially identical and a 35 U.S.C. 103 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 103 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtains prior art products and makes physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Please note that the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether Applicants' injection composition as recited differs and, if so, to what extent, from that of the discussed references. Therefore, with the showing of the references, the burden of establishing non-obviousness by objective evidence is shifted to the Applicants. Therefore, the compositions of the instantly claimed invention, for example, the examples applicant incorporated in the original specification

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experiments 1-5 (pages 4-7) clearly show that applicant's process includes boiling before the addition of *Panax notoginseng saponins* as applicants mentioned and also pasteurization at 110 °C. The incorporation of both the boiling and pasteurization steps in applicants' disclosure is sufficient evidence that the compositions are not structurally affected either by boiling or pasteurization. Absence of evidence to the contrary, the inclusion of the boiling steps by Gai et al., would not result in a structurally different product. Furthermore, although boiling and pasteurization are not strictly synonyms, pasteurization according to Merriam-Webster's Online Dictionary is the partial sterilization of a substance and especially a liquid (as milk) at a temperature and for a period of exposure that destroys objectionable organisms without major chemical alteration of the substance. Therefore, boiling constitutes a means of pasteurization.

Applicants' further argue that it is not obvious to select the specific buffer and the specific pH value as taught in the present application and such selection provides unexpected advantages of the claimed product compared to that of Gai et al, namely, the higher pH stability and thereby the higher stability of the active ingredients of the injections. Applicants also assert the compositions of the present invention possess a surprising stability nowhere foreshadowed by the prior art. In order for the examiner better to understand the improvement secured by the present invention, test results are submitted herewith which showing that the pH value of Xueshuantong injection (i.e., the product of Gai et al) declines remarkably over time while the pH value of the claimed injection show hardly decline. This is a surprising and significant difference.

This is not found persuasive because the comparison data submitted with applicants' remarks will not be considered for unexpected result since all data which applicants wish the examiner to consider for unexpected results must be in the form of an affidavit or declaration (See MPEP § 716, specifically § 716.02(g)). The examiner noticed that the patentability of the instant claims is hinging on the secondary consideration of applicants' comparison data that must be filed in the form of declaration or affidavit.

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Moreover, applicants have only provided the English language abstract of Gai et al. but have not provided either an English language translation or English language equivalent document. Therefore, the examiner would be unable to ascertain whether applicants' data constitutes surprising and/or unexpected results. To determine whether the results are surprising and unexpected, a copy of the English language translation of Gai et al. must be provided by applicants so that the record is clear as to the precise facts what Gai et al. teach in the body of the document with respect to pH stability.

Applicants have not demonstrated how their product is patentably distinct from the cited prior arts nor do the claims as currently written distinguish the instant invention over the prior arts. In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

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shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIGABU KASSA whose telephone number is (571)270-5867. The examiner can normally be reached on 9 am-5 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne P. Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tigabu Kassa

8/13/10

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647